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(54) Title: REGULATION OF HUMAN TRANSIENT RECEPTOR POTENTIAL CHANNEL

(57) Abstract: Reagents which regulate human transient receptor potential channel and reagents which bind to human transient receptor potential channel gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, urinary incontinence, overactive bladder, benign prostatic hyperplasia, lower urinary tract syndromes, and CNS disorders.

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Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

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Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
        115                 120                 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
    130                 135                 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145                 150                 155                 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
                165                 170                 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
            180                 185                 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
        195                 200                 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
    210                 215                 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225                 230                 235                 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
                245                 250                 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
            260                 265                 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
        275                 280                 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
    290                 295                 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305                 310                 315                 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
                325                 330                 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
            340                 345                 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
        355                 360                 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
    370                 375                 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385                 390                 395                 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
                405                 410                 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
            420                 425                 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
        435                 440                 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
    450                 455                 460
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Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625 630 635 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
645 650 655

Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Arg Lys Ile Ile Leu
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
770 775 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785 790 795 800

Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
805 810 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
820 825 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
835 840 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
850 855 860

Phe Ala Val Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865 870 875 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
885 890 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
900 905 910

Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
915 920 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
1010 1015 1020

Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
1025 1030 1035 1040

Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
1045 1050 1055

Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
1060 1065 1070

Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
1075 1080 1085

Glu Ile Ala Asn Lys Ile Lys
1090 1095

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Asp Leu Ser Tyr Ser Glu Ser Asp Leu Val Asn Phe Ile Gln Ala Asn
35 40 45

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Phe Lys Lys Arg Glu Cys Val Phe Phe Ile Lys Asp Ser Lys Ala Thr
 50                  55                  60

Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser Gln His Met Glu Gly
65                  70                  75                  80

Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys
                85                  90                  95

Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly
            100                 105                 110

Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile
        115                 120                 125

Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu
    130                 135                 140

Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg
145                 150                 155                 160

Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly
                165                 170                 175

Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile
            180                 185                 190

Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn
        195                 200                 205

Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp
    210                 215                 220

Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr
225                 230                 235                 240

Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Tyr Ile Leu Asp Asn Asn
                245                 250                 255

His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
            260                 265                 270

Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg
        275                 280                 285

Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe
    290                 295                 300

Ala Gln Gly Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile
305                 310                 315                 320

Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly Ser Gly Gln Ile Ala
                325                 330                 335

Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp Ala Leu Thr Ser Ser
            340                 345                 350

Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro Arg Thr Val Ser Arg
        355                 360                 365

Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile
    370                 375                 380

Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys Met Glu Glu Ala Gly
385                 390                 395                 400

Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala Leu Tyr Lys Ala Phe
                405                 410                 415
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Ser Thr Ser Glu Gln Asp Lys Asp Asn Trp Asn Gly Gln Leu Lys Leu
420 425 430

Leu Leu Glu Trp Asn Gln Leu Asp Leu Ala Asn Asp Glu Ile Phe Thr
435 440 445

Asn Asp Arg Arg Trp Glu Ser Ala Asp Leu Gln Glu Val Met Phe Thr
450 455 460

Ala Leu Ile Lys Asp Arg Pro Lys Phe Val Arg Leu Phe Leu Glu Asn
465 470 475 480

Gly Leu Asn Leu Arg Lys Phe Leu Thr His Asp Val Leu Thr Glu Leu
485 490 495

Phe Ser Asn His Phe Ser Thr Leu Val Tyr Arg Asn Leu Gln Ile Ala
500 505 510

Lys Asn Ser Tyr Asn Asp Ala Leu Leu Thr Phe Val Trp Lys Leu Val
515 520 525

Ala Asn Phe Arg Arg Gly Phe Arg Lys Glu Asp Arg Asn Gly Arg Asp
530 535 540

Glu Met Asp Ile Glu Leu His Asp Val Ser Pro Ile Thr Arg His Pro
545 550 555 560

Leu Gln Ala Leu Phe Ile Trp Ala Ile Leu Gln Asn Lys Lys Glu Leu
565 570 575

Ser Lys Val Ile Trp Glu Gln Thr Arg Gly Cys Thr Leu Ala Ala Leu
580 585 590

Gly Ala Ser Lys Leu Leu Lys Thr Leu Ala Lys Val Lys Asn Asp Ile
595 600 605

Asn Ala Ala Gly Glu Ser Glu Glu Leu Ala Asn Glu Tyr Glu Thr Arg
610 615 620

Ala Val Glu Leu Phe Thr Glu Cys Tyr Ser Ser Asp Glu Asp Leu Ala
625 630 635 640

Glu Gln Leu Leu Val Tyr Ser Cys Glu Ala Trp Gly Gly Ser Asn Cys
645 650 655

Leu Glu Leu Ala Val Glu Ala Thr Asp Gln His Phe Ile Ala Gln Pro
660 665 670

Gly Val Gln Asn Phe Leu Ser Lys Gln Trp Tyr Gly Glu Ile Ser Arg
675 680 685

Asp Thr Lys Asn Trp Lys Ile Ile Leu Cys Leu Phe Ile Ile Pro Leu
690 695 700

Val Gly Cys Gly Phe Val Ser Phe Arg Lys Lys Pro Val Asp Lys His
705 710 715 720

Lys Lys Leu Leu Trp Tyr Tyr Val Ala Phe Phe Thr Ser Pro Phe Val
725 730 735

Val Phe Ser Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe
740 745 750

Ala Tyr Val Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu
755 760 765

Leu Val Leu Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Val Arg
770 775 780

Gln Trp Tyr Val Asn Gly Val Asn Tyr Phe Thr Asp Leu Trp Asn Val
785 790 795 800

Met Asp Thr Leu Gly Leu Phe Tyr Phe Ile Ala Gly Ile Val Phe Arg
805 810 815

Leu His Ser Ser Asn Lys Ser Ser Leu Tyr Ser Gly Arg Val Ile Phe
820 825 830

Cys Leu Asp Tyr Ile Ile Phe Thr Leu Arg Leu Ile His Ile Phe Thr
835 840 845

Val Ser Arg Asn Leu Gly Pro Lys Ile Ile Met Leu Gln Arg Met Leu
850 855 860

Ile Asp Val Phe Phe Phe Leu Phe Leu Phe Ala Val Trp Met Val Ala
865 870 875 880

Phe Gly Val Ala Arg Gln Gly Ile Leu Arg Gln Asn Glu Gln Arg Trp
885 890 895

Arg Trp Ile Phe Arg Ser Val Ile Tyr Glu Pro Tyr Leu Ala Met Phe
900 905 910

Gly Gln Val Pro Ser Asp Val Asp Gly Thr Thr Tyr Asp Phe Ala His
915 920 925

Cys Thr Phe Thr Gly Asn Glu Ser Lys Pro Leu Cys Val Glu Leu Asp
930 935 940

Glu His Asn Leu Pro Arg Phe Pro Glu Trp Ile Thr Ile Pro Leu Val
945 950 955 960

Cys Ile Tyr Met Leu Ser Thr Asn Ile Leu Leu Val Asn Leu Leu Val
965 970 975

Ala Met Phe Gly Tyr Thr Val Gly Thr Val Gln Glu Asn Asn Asp Gln
980 985 990

Val Trp Lys Phe Gln Arg Tyr Phe Leu Val Gln Glu Tyr Cys Ser Arg
995 1000 1005

Leu Asn Ile Pro Phe Pro Phe Ile Val Phe Ala Tyr Phe Tyr Met Val
1010 1015 1020

Val Lys Lys Cys Phe Lys Cys Cys Cys Lys Glu Lys Asn Met Glu Ser
1025 1030 1035 1040

Ser Val Cys Cys Phe Lys Asn Glu Asp Asn Glu Thr Leu Ala Trp Glu
1045 1050 1055

Gly Val Met Lys Glu Asn Tyr Leu Val Lys Ile Asn Thr Lys Ala Asn
1060 1065 1070

Asp Thr Ser Glu Glu Met Arg His Arg Phe Arg Gln Leu Asp Thr Lys
1075 1080 1085

Leu Asn Asp Leu Lys Gly Leu Leu Lys Glu Ile Ala Asn Lys Ile Lys
1090 1095 1100

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Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys Glu Phe
35 40 45

Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly Lys Lys
50 55 60

Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile Leu Tyr
65 70 75 80

Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu Val Ile
85 90 95

Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg Met Arg
100 105 110

Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly Ala Trp
115 120 125

Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile Gly Glu
130 135 140

Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn Ile Val
145 150 155 160

Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp Thr Leu
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Ile Arg Asn Cys Asp Ala Glu Val Pro Val Gly Gln Glu Glu Val Cys
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Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Thr Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys His Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305 310 315 320

Glu Gly Ser Gly Arg Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Pro Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Ser Glu Glu Glu Thr Glu Ser Trp
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625 630 635 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
645 650 655

Gln His Phe Thr Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
770 775 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785 790 795 800

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Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
                805                 810                 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
            820                 825                 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
        835                 840                 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
    850                 855                 860

Phe Ala Val Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865                 870                 875                 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
                885                 890                 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
            900                 905                 910

Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
        915                 920                 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
    930                 935                 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945                 950                 955                 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
                965                 970                 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
            980                 985                 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
        995                 1000                1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
    1010                1015                1020

Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
1025                1030                1035                1040

Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
                1045                1050                1055

Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
            1060                1065                1070

Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
        1075                1080                1085

Glu Ile Ala Asn Lys Ile Lys
    1090                1095
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<210> 16
<211> 1095
<212> PRT
<213> Homo sapiens

<400> 16

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Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
  1               5                  10                  15
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Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625 630 635 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
645 650 655

Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
660 665 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
675 680 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
690 695 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
705 710 715 720

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
770 775 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785 790 795 800

Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
805 810 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
820 825 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
835 840 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
850 855 860

Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865 870 875 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
885 890 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
900 905 910

Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
915 920 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
1010 1015 1020

Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
1025 1030 1035 1040

Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
1045 1050 1055

Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
1060 1065 1070

Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
1075 1080 1085

Glu Ile Ala Asn Lys Ile Lys
1090 1095

<210> 17
<211> 652
<212> PRT
<213> Homo sapiens

<400> 17
Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625 630 635 640

Ala Trp Gly Gly Leu Glu His His His His His His
645 650

<210> 18
<211> 1095
<212> PRT
<213> Homo sapiens

<400> 18

Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

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Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
        355                 360                 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
    370                 375                 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385                 390                 395                 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
                405                 410                 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
            420                 425                 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
        435                 440                 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
    450                 455                 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465                 470                 475                 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
                485                 490                 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
            500                 505                 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
        515                 520                 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
    530                 535                 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545                 550                 555                 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
                565                 570                 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
            580                 585                 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
        595                 600                 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
    610                 615                 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625                 630                 635                 640

Ala Trp Gly Gly Ser Asn Cys Leu Glu Leu Ala Val Glu Ala Thr Asp
                645                 650                 655

Gln His Phe Ile Ala Gln Pro Gly Val Gln Asn Phe Leu Ser Lys Gln
            660                 665                 670

Trp Tyr Gly Glu Ile Ser Arg Asp Thr Lys Asn Trp Lys Ile Ile Leu
        675                 680                 685

Cys Leu Phe Ile Ile Pro Leu Val Gly Cys Gly Phe Val Ser Phe Arg
    690                 695                 700

Lys Lys Pro Val Asp Lys His Lys Lys Leu Leu Trp Tyr Tyr Val Ala
705                 710                 715                 720
```

Phe Phe Thr Ser Pro Phe Val Val Phe Ser Trp Asn Val Val Phe Tyr
725 730 735

Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val Leu Leu Met Asp Phe His
740 745 750

Ser Val Pro His Pro Pro Glu Leu Val Leu Tyr Ser Leu Val Phe Val
755 760 765

Leu Phe Cys Asp Glu Val Arg Gln Trp Tyr Val Asn Gly Val Asn Tyr
770 775 780

Phe Thr Asp Leu Trp Asn Val Met Asp Thr Leu Gly Leu Phe Tyr Phe
785 790 795 800

Ile Ala Gly Ile Val Phe Arg Leu His Ser Ser Asn Lys Ser Ser Leu
805 810 815

Tyr Ser Gly Arg Val Ile Phe Cys Leu Asp Tyr Ile Ile Phe Thr Leu
820 825 830

Arg Leu Ile His Ile Phe Thr Val Ser Arg Asn Leu Gly Pro Lys Ile
835 840 845

Ile Met Leu Gln Arg Met Leu Ile Asp Val Phe Phe Phe Leu Phe Leu
850 855 860

Phe Ala Xaa Trp Met Val Ala Phe Gly Val Ala Arg Gln Gly Ile Leu
865 870 875 880

Arg Gln Asn Glu Gln Arg Trp Arg Trp Ile Phe Arg Ser Val Ile Tyr
885 890 895

Glu Pro Tyr Leu Ala Met Phe Gly Gln Val Pro Ser Asp Val Asp Gly
900 905 910

Thr Thr Tyr Asp Phe Ala His Cys Thr Phe Thr Gly Asn Glu Ser Lys
915 920 925

Pro Leu Cys Val Glu Leu Asp Glu His Asn Leu Pro Arg Phe Pro Glu
930 935 940

Trp Ile Thr Ile Pro Leu Val Cys Ile Tyr Met Leu Ser Thr Asn Ile
945 950 955 960

Leu Leu Val Asn Leu Leu Val Ala Met Phe Gly Tyr Thr Val Gly Thr
965 970 975

Val Gln Glu Asn Asn Asp Gln Val Trp Lys Phe Gln Arg Tyr Phe Leu
980 985 990

Val Gln Glu Tyr Cys Ser Arg Leu Asn Ile Pro Phe Pro Phe Ile Val
995 1000 1005

Phe Ala Tyr Phe Tyr Met Val Val Lys Lys Cys Phe Lys Cys Cys Cys
1010 1015 1020

Lys Glu Lys Asn Met Glu Ser Ser Val Cys Cys Phe Lys Asn Glu Asp
1025 1030 1035 1040

Asn Glu Thr Leu Ala Trp Glu Gly Val Met Lys Glu Asn Tyr Leu Val
1045 1050 1055

Lys Ile Asn Thr Lys Ala Asn Asp Thr Ser Glu Glu Met Arg His Arg
1060 1065 1070

Phe Arg Gln Leu Asp Thr Lys Leu Asn Asp Leu Lys Gly Leu Leu Lys
1075 1080 1085

Glu Ile Ala Asn Lys Ile Lys
1090 1095

<210> 19
<211> 652
<212> PRT
<213> Homo sapiens

<400> 19
Met Arg Asn Arg Arg Asn Asp Thr Leu Asp Ser Thr Arg Thr Leu Tyr
1 5 10 15

Ser Ser Ala Ser Arg Ser Thr Asp Leu Ser Tyr Ser Glu Ser Asp Leu
20 25 30

Val Asn Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe
35 40 45

Thr Lys Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala
50 55 60

Gln Ser Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp
65 70 75 80

Asn Tyr Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp
85 90 95

Ile Gln Phe Glu Thr Leu Gly Lys Lys Gly Lys Tyr Ile Arg Leu Ser
100 105 110

Cys Asp Thr Asp Ala Glu Ile Leu Tyr Glu Leu Leu Thr Gln His Trp
115 120 125

His Leu Lys Thr Pro Asn Leu Val Ile Ser Val Thr Gly Gly Ala Lys
130 135 140

Asn Phe Ala Leu Lys Pro Arg Met Arg Lys Ile Phe Ser Arg Leu Ile
145 150 155 160

Tyr Ile Ala Gln Ser Lys Gly Ala Trp Ile Leu Thr Gly Gly Thr His
165 170 175

Tyr Gly Leu Met Lys Tyr Ile Gly Glu Val Val Arg Asp Asn Thr Ile
180 185 190

Ser Arg Ser Ser Glu Glu Asn Ile Val Ala Ile Gly Ile Ala Ala Trp
195 200 205

Gly Met Val Ser Asn Arg Asp Thr Leu Ile Arg Asn Cys Asp Ala Glu
210 215 220

Gly Tyr Phe Leu Ala Gln Tyr Leu Met Asp Asp Phe Thr Arg Asp Pro
225 230 235 240

Leu Tyr Ile Leu Asp Asn Asn His Thr His Leu Leu Leu Val Asp Asn
245 250 255

Gly Cys His Gly His Pro Thr Val Glu Ala Lys Leu Arg Asn Gln Leu
260 265 270

Glu Lys Tyr Ile Ser Glu Arg Thr Ile Gln Asp Ser Asn Tyr Gly Gly
275 280 285

Lys Ile Pro Ile Val Cys Phe Ala Gln Gly Gly Gly Lys Glu Thr Leu
290 295 300

Lys Ala Ile Asn Thr Ser Ile Lys Asn Lys Ile Pro Cys Val Val Val
305 310 315 320

Glu Gly Ser Gly Gln Ile Ala Asp Val Ile Ala Ser Leu Val Glu Val
325 330 335

Glu Asp Ala Leu Thr Ser Ser Ala Val Lys Glu Lys Leu Val Arg Phe
340 345 350

Leu Pro Arg Thr Val Ser Arg Leu Pro Glu Glu Glu Thr Glu Ser Trp
355 360 365

Ile Lys Trp Leu Lys Glu Ile Leu Glu Cys Ser His Leu Leu Thr Val
370 375 380

Ile Lys Met Glu Glu Ala Gly Asp Glu Ile Val Ser Asn Ala Ile Ser
385 390 395 400

Tyr Ala Leu Tyr Lys Ala Phe Ser Thr Ser Glu Gln Asp Lys Asp Asn
405 410 415

Trp Asn Gly Gln Leu Lys Leu Leu Leu Glu Trp Asn Gln Leu Asp Leu
420 425 430

Ala Asn Asp Glu Ile Phe Thr Asn Asp Arg Arg Trp Glu Ser Ala Asp
435 440 445

Leu Gln Glu Val Met Phe Thr Ala Leu Ile Lys Asp Arg Pro Lys Phe
450 455 460

Val Arg Leu Phe Leu Glu Asn Gly Leu Asn Leu Arg Lys Phe Leu Thr
465 470 475 480

His Asp Val Leu Thr Glu Leu Phe Ser Asn His Phe Ser Thr Leu Val
485 490 495

Tyr Arg Asn Leu Gln Ile Ala Lys Asn Ser Tyr Asn Asp Ala Leu Leu
500 505 510

Thr Phe Val Trp Lys Leu Val Ala Asn Phe Arg Arg Gly Phe Arg Lys
515 520 525

Glu Asp Arg Asn Gly Arg Asp Glu Met Asp Ile Glu Leu His Asp Val
530 535 540

Ser Pro Ile Thr Arg His Pro Leu Gln Ala Leu Phe Ile Trp Ala Ile
545 550 555 560

Leu Gln Asn Lys Lys Glu Leu Ser Lys Val Ile Trp Glu Gln Thr Arg
565 570 575

Gly Cys Thr Leu Ala Ala Leu Gly Ala Ser Lys Leu Leu Lys Thr Leu
580 585 590

Ala Lys Val Lys Asn Asp Ile Asn Ala Ala Gly Glu Ser Glu Glu Leu
595 600 605

Ala Asn Glu Tyr Glu Thr Arg Ala Val Glu Leu Phe Thr Glu Cys Tyr
610 615 620

Ser Ser Asp Glu Asp Leu Ala Glu Gln Leu Leu Val Tyr Ser Cys Glu
625 630 635 640

Ala Trp Gly Gly Leu Glu His His His His His His
645 650

<210> 20
<211> 1104
<212> PRT
<213> Homo sapiens

<400> 20
Met Ser Phe Arg Ala Ala Arg Leu Ser Met Arg Asn Arg Arg Asn Asp
1 5 10 15

Thr Leu Asp Ser Thr Arg Thr Leu Tyr Ser Ser Ala Ser Arg Ser Thr
20 25 30

Asp Leu Ser Tyr Ser Glu Ser Asp Leu Val Asn Phe Ile Gln Ala Asn
35 40 45

Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys Asp Ser Lys Ala Thr
50 55 60

Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser Gln His Met Glu Gly
65 70 75 80

Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr Lys Lys His Thr Lys
85 90 95

Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln Phe Glu Thr Leu Gly
100 105 110

Lys Lys Gly Lys Tyr Ile Arg Leu Ser Cys Asp Thr Asp Ala Glu Ile
115 120 125

Leu Tyr Glu Leu Leu Thr Gln His Trp His Leu Lys Thr Pro Asn Leu
130 135 140

Val Ile Ser Val Thr Gly Gly Ala Lys Asn Phe Ala Leu Lys Pro Arg
145 150 155 160

Met Arg Lys Ile Phe Ser Arg Leu Ile Tyr Ile Ala Gln Ser Lys Gly
165 170 175

Ala Trp Ile Leu Thr Gly Gly Thr His Tyr Gly Leu Met Lys Tyr Ile
180 185 190

Gly Glu Val Val Arg Asp Asn Thr Ile Ser Arg Ser Ser Glu Glu Asn
195 200 205

Ile Val Ala Ile Gly Ile Ala Ala Trp Gly Met Val Ser Asn Arg Asp
210 215 220

Thr Leu Ile Arg Asn Cys Asp Ala Glu Gly Tyr Phe Leu Ala Gln Tyr
225 230 235 240

Leu Met Asp Asp Phe Thr Arg Asp Pro Leu Cys Ile Leu Asp Asn Asn
245 250 255

His Thr His Leu Leu Leu Val Asp Asn Gly Cys His Gly His Pro Thr
260 265 270

Val Glu Ala Lys Leu Arg Asn Gln Leu Glu Lys Tyr Ile Ser Glu Arg
275 280 285

Thr Ile Gln Asp Ser Asn Tyr Gly Gly Lys Ile Pro Ile Val Cys Phe
290 295 300

Ala Gln Gly Gly Gly Lys Glu Thr Leu Lys Ala Ile Asn Thr Ser Ile
305 310 315 320

Lys Asn Lys Ile Pro Cys Val Val Val Glu Gly Ser Gly Gln Ile Ala
325 330 335

Asp Val Ile Ala Ser Leu Val Glu Val Glu Asp Ala Leu Thr Ser Ser
340 345 350

Ala Val Lys Glu Lys Leu Val Arg Phe Leu Pro Arg Thr Val Ser Arg
355 360 365

Leu Pro Glu Glu Glu Thr Glu Ser Trp Ile Lys Trp Leu Lys Glu Ile
370 375 380

Leu Glu Cys Ser His Leu Leu Thr Val Ile Lys Met Glu Glu Ala Gly
385 390 395 400

Asp Glu Ile Val Ser Asn Ala Ile Ser Tyr Ala Leu Tyr Lys Ala Phe
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<213> Homo sapiens

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Phe Ile Gln Ala Asn Phe Lys Lys Arg Glu Cys Val Phe Phe Thr Lys
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Asp Ser Lys Ala Thr Glu Asn Val Cys Lys Cys Gly Tyr Ala Gln Ser
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Gln His Met Glu Gly Thr Gln Ile Asn Gln Ser Glu Lys Trp Asn Tyr
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Lys Lys His Thr Lys Glu Phe Pro Thr Asp Ala Phe Gly Asp Ile Gln
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820 825 830

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835 840 845

Trp Asn Val Val Phe Tyr Ile Ala Phe Leu Leu Leu Phe Ala Tyr Val
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Leu Leu Met Asp Phe His Ser Val Pro His Pro Pro Glu Leu Val Leu
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Tyr Ser Leu Val Phe Val Leu Phe Cys Asp Glu Lys Arg Lys Thr Ala
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900 905 910

Phe Leu Met Ile Ser Arg Ser Phe Arg Gly Glu Glu Met Ser Ile Gly
915 920 925

Lys Gln His
930

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(74) Common Representative: **BAYER HEALTHCARE AG**; Law and Patents, Patents and Licensing, 51368 Leverkusen (DE).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:
— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*
— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii)) for all designations*

Published:
— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

(88) Date of publication of the international search report: 10 June 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: REGULATION OF HUMAN TRANSIENT RECEPTOR POTENTIAL CHANNEL

(57) Abstract: Reagents which regulate human transient receptor potential channel and reagents which bind to human transient receptor potential channel gene products can play a role in preventing, ameliorating, or correcting dysfunctions or diseases including, but not limited to, urinary incontinence, overactive bladder, benign prostatic hyperplasia, lower urinary tract syndromes, and CNS disorders.

WO 2003/087158 A3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/03713

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/70 C12Q1/68 G01N33/68 C07K14/705

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 03/064602 A (NEUHAUSSER WERNER M ;JULIUS DAVID (US); MCKEMY DAVID D (US); UNIV) 7 August 2003 (2003-08-07) the whole document	1-8
P,X	WO 02/101045 A (IRM LLC ;NOVARTIS AG (CH); GANJU PAMPOSH (GB); BEVAN STUART (GB);) 19 December 2002 (2002-12-19) SEQ ID Nos 8 and 11	1-8
P,X	WO 02/087608 A (BOEHRINGER INGELHEIM PHARMA ;KRESS MICHAELA (DE); HABERBERGER RAIN) 7 November 2002 (2002-11-07) claims	1-8
P,X	WO 02/44210 A (SQUIBB BRISTOL MYERS CO (US)) 6 June 2002 (2002-06-06) claims 17-20,25	1-8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2004	15. 04. 2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Routledge, B

Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 02/10391 A (CURTIS RORY A J ;MILLENNIUM PHARM INC (US)) 7 February 2002 (2002-02-07) claims 17-26	1-8
X	WO 02/10382 A (WISSENBACH ULRICH) 7 February 2002 (2002-02-07) claim 31 page 17, paragraph 6 - page 19, paragraph 1	1-8
X	WO 02/04520 A (INCYTE GENOMICS INC) 17 January 2002 (2002-01-17) claims 19,20,22,23,25-27	1-8
X	WO 02/02633 A (INCYTE GENOMICS INC ;TRIBOULEY CATHERINE M (US); RAUMANN BRIGITTE) 10 January 2002 (2002-01-10) claims 19,20,22,23,25-27	1-8
X	WO 02/00722 A (SILOS SANTIAGO INMACULADA ;CURTIS RORY A J (US); MILLENNIUM PHARM) 3 January 2002 (2002-01-03) Seq ID No.5claim 2 page 137 - page 140	1-8
X	WO 02/00718 A (SILOS SANTIAGO INMACULADA ;CURTIS RORY A J (US); MILLENNIUM PHARM) 3 January 2002 (2002-01-03) claims 17-35 page 2, line 34 - page 3, line 3 page 4, line 1 - line 29	1-8
X	WO 01/077331 A (MILLENIUM PHARMACEUTICALS INC ;SILOS SANTIAGO INMACULADA (US); CUR) 18 October 2001 (2001-10-18) claims 10-22,28-30 page 3, line 15 - line 25 page 7, line 1 - line 19 page 8, line 17 - line 23	1-8
X	WO 01/068698 A (BOEHRINGER INGELHEIM) 20 September 2001 (2001-09-20) claims 43-57,68 page 28, line 25 - page 34, line 34	1-8
X	WO 01/062794 A (LORA JOSE M ;CURTIS RORY A J (US); GLUCKSMANN MARIA ALEXANDRA (US)) 30 August 2001 (2001-08-30) claims 17-30,37,38 page 7, line 10 - line 21 page 12, line 17 - line 25 page 13, line 11 - line 16	1-8

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 03/03713

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 01/046258 A (INCYTE GENOMICS INC ;AZIMZAI YALDA (US); KHAN FARRAH A (US); REDDY) 28 June 2001 (2001-06-28) claims 19,20,22,23,25-27	1-8
X	WO 00/40614 A (BETH ISRAEL HOSPITAL ;SCHARENBERG ANDREW M (US)) 13 July 2000 (2000-07-13) claims 24,36,37	1-8
X	WO 00/04929 A (UNIV SOUTH ALABAMA) 3 February 2000 (2000-02-03) page 7, line 6 - line 12 page 15, line 12 - line 26	1-8
X	WO 99/09140 A (BRAKE ANTHONY (US); JULIUS DAVID (US); UNIV.CALIFORNIA(US); CATERINA M) 25 February 1999 (1999-02-25) claim 19	1-8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/03713

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 1-8
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-8 (partially)

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-8

Given the breadth of the independent claims due to the definitions of the sequences which includes sequences of anything from 26% identity upwards, the initial phase of the search revealed a very large number of documents relevant to the issue of novelty. So many documents were retrieved that it is impossible to determine which parts of the claim(s) may be said to define subject-matter for which protection might legitimately be sought (Article 6 PCT). For these reasons, a meaningful search over the whole breadth of the claim(s) is impossible. Consequently, the search has been restricted to methods of screening using SEQ ID No.12.

Present claims 1-4 relate to an extremely large number of possible methods. Support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT is not to be found, as the description merely represents a theoretical approach and does not exemplify the invention in practice. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely methods of screening using SEQ ID No.12.

Present claims 5-8 relate to a reagent and uses therefof defined by reference to a desirable characteristic or property, namely that the reagewnt has been identified using the screening methods of claims 1-4.

The claims cover all reagents having this characteristic or property, including known compounds (page 38 line 25) whereas the application provides does not provide support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for a single reagent as no specific reagents are identified. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product/compound/method/apparatus by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the use of SEQ ID No.12.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Other documents relating to disclosure concerning transient receptor potential channels have also been added to the search report in order to illustrate the state of the art. However the list is not exhaustive and further documents may become relevant when the subject matter of the claims has been amended to overcome the above objections.

The applicant's attention is drawn to the fact that claims relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure. If the application proceeds into the regional phase before the EPO, the applicant is reminded that a search may be carried out during examination before the EPO (see EPO Guideline C-VI, 8.5), should the problems which led to the Article 17(2) declaration be overcome.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-8 (partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.12 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

---

2. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.13 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

---

3. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.14 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

---

4. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.15 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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5. claims: 1-8 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.16 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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6. claims: 1-8 (partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.17 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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7. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.18 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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8. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.19 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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9. claims: 1-8(partially)

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.20 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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10. claims: 1-8(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising a test compound with a polynucleotide for human transient receptor channel encoding the amino acid sequence SEQ ID No.21 or complement, derivative or fragment thereof, reagent so identified, composition containing said agent, use of composition comprising said agent.

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11. claims: 1-8 (partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.1 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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12. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.2 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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13. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.3 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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14. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.4 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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15. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.5 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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16. claims: 1-8(partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.6 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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17. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.7 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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18. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.8 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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19. claims: 1-8(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.9 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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20. claims: 1-18(partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.10 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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21. claims: 1-8 (partially)

Method of screening comprising contacting a test compound with a polynucleotide for human transient receptor channel comprising SEQ ID No.11 or complement, derivative or fragment thereof, reagent so identified, composition containing said reagent, use of composition comprising said reagent.

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